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Mental disorders in chronic obstructive pulmonary disease (COPD)

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This paper is dedicated to the memory of the first author's father, Karl Vögele

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Summary

Recent research using questionnaire measures has demonstrated high prevalence rates of mental disorders in chronic obstructive pulmonary disease (COPD). However, clinical interviews and clinical rather than healthy control groups have rarely been employed. The aim of the present study was to assess mental disorders in patients with COPD with advanced methodology, to identify moderating factors explaining mental co-morbidities and to compare results with a clinical control group without COPD.

A standardized clinical interview (F-DIPS) and a range of questionnaires were used to assess mental disorders, perceived physical symptoms and cognitions in 20 hospitalized patients with mild-to-moderate COPD (mean FEV₁/VC (%) = 61.3). Results were compared with a hospitalized clinical control group without pulmonary dysfunction (CCG; *N* = 20). Results showed that 55% of patients with COPD received a diagnosis of a mental disorder compared to 30% of CCG patients. All principal mental diagnoses in the COPD group were anxiety disorders (especially Panic Disorder with Agoraphobia), while CCG patients received a wider range of diagnoses (anxiety, pain, alcohol abuse). There was no systematic association between anxiety levels and respiratory function in the whole COPD group, but a positive correlation between anxiety levels and perceived physical symptoms ($p < 0.001$) as well as negative cognitions ($p < 0.001$ and $p < 0.05$, respectively) for COPD patients with anxiety disorder (*N* = 11).

The present results confirm the high prevalence rate of anxiety in patients with COPD and suggest further that anxiety in COPD patients may be mediated by cognitive processes. These findings are discussed in terms of their implications for treatment.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic progressive condition characterized by a slowly progressive irreversible bronchial obstruction and a fluctuating symptom complex of recurrent productive cough and dyspnea¹ and a worldwide leading cause of morbidity and mortality.^{2–4} Due to the irreversible nature of COPD, the aim of treatment in patients with COPD is not to cure but to reduce symptoms, increase functioning, and improve the patients' quality of life.^{1,5}

It has long been suggested that emotional disturbances such as depression and anxiety are common among patients with COPD,^{6–17} which obviously has a detrimental effect on quality of life as they affect emotional, social and physical functioning. Recent systematic reviews reported prevalence rates ranging from 2% to 57% for depression and 2% to 51% for anxiety in patients with COPD.^{18,19} However, these and other authors conclude that the empirical evidence for a significant risk of depression and anxiety in this patient group remains inconclusive because of the poor methodological quality of most of the published studies (e.g., lack of adequate control groups, small sample sizes, variability in instruments and cut off scores used to measure depression and anxiety).^{6,18,19} Interestingly, Van Manen et al.⁷ found no relationship between increased depression scores and pulmonary function (FEV₁% predicted), indicating a weak or perhaps non-linear association between clinical measures of pulmonary function and depressive symptoms. However, the risk of depression was significantly increased by factors such as living alone, perceived severity of symptoms and self-reported impaired physical function suggesting a mediating role of illness perception for depressive symptoms.

It becomes clear that our knowledge about psychological ramifications of COPD is still limited. The first issue concerns the assessment of mental disorders in patients with COPD. Studies have tended to use questionnaire based self-report measures rather than clinical interviews to assess depression and anxiety in COPD patients. For example, only 4 out of 14 studies listed in the review by Brenes¹⁹ used standard diagnostic procedures employing DSM criteria to assess anxiety disorders. While the use of self-report measures is economical and allows for large samples to be screened, it is difficult to interpret questionnaire-based results in terms of their clinical significance for two reasons: firstly, studies have used a variety of instruments and cut off scores to determine the level of depression and anxiety making comparisons between studies difficult. Secondly, questionnaire items designed to measure anxiety and depression may overlap with symptoms that are primarily associated with the physical symptoms of the medical condition, potentially leading to misdiagnoses and therefore overestimations of the prevalence rates of mental disorders in this patient population.

A further issue concerns the question of specificity of anxiety and depression for COPD. Depression and anxiety have been shown to be associated with other chronic conditions such as cardiovascular disorders, diabetes and stroke.²⁰ As these studies have shown it is important to consider alternative explanations for any observed association between mental disorders and chronic physical conditions. For example, anxiety and depression may be a

temporary adjustment as a result of the diagnosis of a potentially life threatening and/or incurable disease; they could also be the result of patients being hospitalized at the time of investigation. However, almost all of the very few studies which employed a controlled design used healthy controls. Only one study¹⁵ used a random sample of geriatric patients including those with COPD and other chronic conditions allowing for comparisons between these groups. However, Kvaal et al.¹⁵ only used the State-Trait Anxiety Inventory (STAI) questionnaire to assess anxiety making it difficult to arrive at firm conclusions about the clinical significance of their findings.

A first aim of the current investigation was, therefore, to address these issues by using a clinical standardized interview in order to assess mental co-morbidity in hospitalized patients diagnosed with COPD. Employing DSM-IV criteria this interview allows for differentiation of subtypes of mental disorders which could contribute to improvements in treatment approaches in patients with COPD. A second aim was to examine the specificity of any mental disorder for COPD. Therefore, chronically ill patients who were also hospitalized at the time of investigation but who had no COPD related symptoms were used as a clinical control group (CCG).

Given the previously reported elevated prevalence rates for anxiety disorders in COPD patients it would seem important to identify any factors explaining these findings. Cognitive-behavioral models of anxiety and in particular panic disorder implicate the role of catastrophic misinterpretations of physical sensations in the etiology and maintenance of panic attacks.²¹ When patients with COPD experience dyspnea, they may make incorrect interpretations (e.g. "I am going to die") in response to the feeling of breathlessness. This in turn leads to heightened physiological arousal, followed by additional sensations and misinterpretations. While breathlessness may represent actual danger in patients with COPD, COPD patients with panic disorder have more negative cognitions than those not experiencing panic attacks. In previous studies, e.g.^{14,22} no association could be found between anxiety levels and objective measures of lung function impairment suggesting that anxiety in COPD patients with panic disorder reflects inaccurate cognitions rather than greater disease severity. The third aim of the present study was, therefore, to investigate any differences in agoraphobic and panic cognitions, symptom perception and measures of pulmonary function between COPD patients with and without anxiety disorders.

In summary, we hypothesized that (1) there is a higher percentage of mental disorders in hospitalized patients with COPD compared to a hospitalized CCG, and (2) anxiety levels in COPD patients are associated with negative cognitions and symptom perception but not with measures of pulmonary function.

Methods

Participants

We examined 20 patients with mild-to-moderate COPD (mean FEV₁/VC (%) = 61.3, S.D. = 5.9) being hospitalized

Table 1 Socio-demographic and medical characteristics of COPD and clinical control group (CCG) patients.

	COPD (n = 20)	CCG (n = 20)	p
Male gender (n)	14 (70%)	15 (75%)	ns
Mean age (S.D.) (year)	62.2 (10.0)	52.7 (13.0)	0.05
Retired (n)	13 (65%)	11 (55%)	ns
Living alone (n)	3 (15%)	2 (10%)	ns
Duration of primary medical condition (S.D.) (year)	14.1 (9.8)	9.7 (6.5)	ns
FEV ₁ /VC (%)	61.3 (5.9)	–	–
FEV ₁ % predicted	75.1 (9.0)	–	–

at the time of investigation because of exacerbation episodes since anxiety and depression seem to be particularly prominent during periods of symptom aggravation.^{15,23} Eligibility criteria included age > 18 years, German-speaking, a clinically confirmed primary diagnosis of COPD and patients' agreement to participate. Patients were excluded from participation if they had other co-morbid conditions which have been shown to be associated with elevated anxiety and depression (e.g., coronary heart disease, stroke, cancer and dementia) and thus, would have had an additional impact on the psychological measurements unrelated to COPD. The CCG consisted of 20 patients being hospitalized at the time of investigation because of degenerative orthopaedic conditions (e.g. osteoarthritis). Eligibility criteria were similar to those for the COPD patient group, except that patients in this group were excluded if any co-morbid condition with lung function impairment was present (e.g. COPD, asthma). Study participants meeting the inclusion criteria for the COPD or CCG were recruited consecutively from those admitted to hospital over the study period. Sample characteristics of the two groups are summarized in Table 1.

Measures

Medical assessment

For both groups information on patients' medical history was drawn from the medical records. These data included primary diagnosis for hospital referral, disease course and duration, co-morbid medical conditions and current medication. In COPD patients, diagnostic status was confirmed by lung function measurements (FEV₁/VC (%), r_{tot}) carried out in accordance with established guidelines²⁴ and by arterial blood gas analyses (PaO₂).

Clinical diagnostic interview (F-DIPS)

Diagnostic assessments were based on the "Diagnostisches Interview für Psychische Störungen—Forschungsversion" (F-DIPS, Diagnostic Interview for Psychiatric Disorders—Research Version).²⁵ The F-DIPS is a well standardized, validated and structured interview allowing the assessment of mental disorders on Axis I of the DSM-IV,²⁶ and is based on

the Anxiety Disorders Interview Schedule (ADIS-IV-L).²⁷ DIPS yields lifetime-, period-, and point-prevalence rates for the following mental disorders: all anxiety disorders, all affective disorders, hypochondrias, somatization disorder, conversion disorder and pain disorder, substance abuse and dependence, bulimia nervosa and anorexia nervosa. F-DIPS interviews were conducted by a trained clinical psychologist. Written interview transcripts were scored and diagnoses awarded by another trained psychologist who was blind to interviewees' medical condition.

As study participants were admitted to hospital because of their medical condition a principal DSM-IV diagnosis was established on the basis of individual's assessment which mental condition they experienced as the most stressful and would, therefore, seek treatment for first. In addition to current diagnoses and to extend our findings beyond exacerbation periods, it was assessed during the interviews whether participants met diagnostic criteria in the past (prior history).

In an attempt to distinguish between symptoms primarily associated with a medical condition and those occurring during, e.g. a panic attack, patients were asked to describe the specific circumstances in which they experienced symptoms such as palpitations, shortness of breath, trembling, feeling dizzy, sweating, fatigue, etc. Only symptoms that were reported to occur outside exacerbation episodes and primarily in the absence of a worsening of the medical condition were counted towards DSM criteria. In order to verify that reported symptoms occurred in the absence of a worsening of the medical condition patients' medical records (containing physicians' notes on when exacerbation periods occurred) were checked against patients' self-report. In addition, patients' descriptions of the specific circumstances in which symptoms occurred were discussed with a physician to ensure that symptoms could not be explained in terms of COPD, e.g. by differentiating between common physical triggers of dyspnea such as exercise or exposure to noxious agents from common emotional triggers such as sudden panic attacks or stress.

Symptom Checklist-90-Revised (SCL-90-R)

The SCL-90-R,²⁸ German version,²⁹ is a well-standardized and validated 90-item questionnaire assessing nine primary symptom dimensions and a Global Severity Index (GSI), based on all 90 items. Primary symptom dimensions include somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism which refer to the preceding 6 months. The GSI is used to measure the intensity of perceived distress. Two further main indices can be aggregated from the SCL-90-R: positive symptom distress (PSD), which measures the intensity of all answers and the positive symptom total (PST), which describes the number of above listed symptoms a person is suffering from. The SCL-90-R is frequently used as an accompaniment to interview-derived clinical classification providing a quantitative, continuous measure of psychopathology.

Self-Report Inventory for Somatic Symptoms (SISS)

In its original form, the SISS is a standardized and validated paper and pencil self-report measure, which assesses the

experience and intensity of physical sensations pertaining to the cardiovascular and gastrointestinal system.³⁰ For the current investigation an adapted version was used with items added to include the musculoskeletal and respiratory systems. Participants were asked to indicate on a scale from 1 (not aware at all) to 7 (extremely aware) to what extent they are frequently aware of physical sensations (e.g. beating heart, stomach cramps, muscle tension, airway obstruction) emanating from these body systems. Average symptom perception scores for the four body systems were calculated and, in addition, a total average score was computed across all items to represent a general measure of intensity of symptom perception.

Questionnaire on knowledge and worries about COPD

The first part of this self-constructed questionnaire was designed to assess COPD patients' perceived and actual knowledge about COPD (in the interest of brevity these data are not presented here). The second part of the questionnaire assesses worries and physical sensations when experiencing difficulty in breathing. In particular, patients are asked to describe the physical sensations they experience and typical thoughts occurring during an acute episode of breathlessness in a free-response format. Interpretative phenomenological analysis (IPA)^{31,32} resulted in four main themes: fear of fear, fear of dying, staying calm, and seeking help. For further analyses individual responses were scored in a yes–no format depending on whether it was endorsed. This analysis was carried out by two independent raters who were experienced in IPA and blind to any results from the clinical diagnostic interview. Finally, participants were asked to indicate on a visual analogue scale³³ their subjective experience of breathlessness ("how much do you suffer from breathlessness?") with the anchor points "not at all" and "extremely".

Procedure

Patients in the two study groups were recruited from two separate wards specialized in respiratory and orthopaedic conditions, respectively, of the same medium sized district general hospital. Patients meeting the inclusion criteria were contacted by a trained psychologist on their hospital ward and provided informed written consent. The interview sessions took place after patients were stable again, i.e. on average 4–5 days after hospital admission. At the beginning, patients were asked to complete the self-report questionnaires and offered help with filling-in the forms if they wished. This was followed by the clinical interview (F-DIPS). Assessment materials were identical for both patient groups with the exception of the questionnaire on knowledge and worries about COPD which was administered to COPD patients only. Those receiving a DSM-IV diagnosis were offered referral to clinical psychological services. The study procedure received ethical approval from the hospitals' ethics boards.

Data analysis

Group comparisons on dichotomous data (number of diagnoses awarded, panic/agoraphobic cognitions) were

carried out using χ^2 -tests and Fisher's exact test. Data on interval scale level (SCL-90-R, SISS, pulmonary function parameters, perceived breathlessness) were analyzed using multivariate analysis of variance (MANOVA) with one grouping factor and—if significant—subsequent univariate comparisons between groups. Group differences in perceived worries and physical sensations were analyzed non-parametrically using Mann–Whitney *U*-tests. For identification of predictors of anxiety levels, a multiple regression was performed using the anxiety scale of the SCL-90-R as dependent variable and the total symptom perception score of the SISS and agoraphobic/panic cognitions (fear of fear, fear of dying) as independent variables. A significance level of $p = 0.05$ was applied for all statistical tests.

Results

Differences in DSM-IV diagnoses, SCL-90-R and SISS between COPD and CCG

Table 2 gives details of current principal DSM-IV axis I diagnoses for COPD and CCG groups by case. In addition, current co-morbid as well as past diagnoses ("prior history") are listed. Only those study participants are listed who received a current and/or past diagnosis. More than half of all participating COPD patients (55%) received a primary diagnosis for a mental disorder compared to 30% in the CCG group ($p = 0.055$). There was a significant difference between groups in the number of patients with the principal diagnosis "anxiety disorders": all of the principal diagnoses awarded in the COPD group were anxiety disorders ($n = 11$) compared to four patients with anxiety disorders in the CCG group ($p < 0.05$). The most common anxiety disorder subtype in COPD patients was Panic Disorder with Agoraphobia (eight out of 11 anxiety disorder diagnoses) followed by Specific Phobia (situational type, $n = 2$) and one case of Social Phobia. In the CCG group there were two cases of panic disorder with and without agoraphobia, respectively, and one case each of Social Phobia and Specific Phobia (Blood–Injection–Injury type). The two remaining non-anxiety disorder diagnoses in the CCG group were one case of Alcohol Use Disorder and one case of Pain Disorder.

Groups did not differ significantly in the number of current co-morbid diagnoses, and the number of cases with past diagnoses was identical between groups ($n = 5$ each). Although the number of past anxiety diagnoses was higher in the COPD group ($n = 3$) than in the CCG ($n = 1$) this difference was not significant. However, correlation analyses of past and current diagnoses using Φ as association index revealed a significant association across the whole sample ($\Phi = 0.32$, $p < 0.05$). Separate analyses performed for each group revealed a significant association between past and current DSM diagnoses in the COPD group only ($\Phi = 0.52$, $p < 0.05$), indicating continuing psychological symptom distress in COPD patients with a current diagnosis.

Table 3 summarizes means, S.D. and p -values for SCL-90-R and SISS factors for both groups. MANOVA including SCL-90-R primary symptom dimensions and SISS scales (excluding the SCL-90-R summary scores and the SISS total symptom perception score as they are not independent) revealed a significant main effect for group ($p < 0.001$). Univariate

Table 2 DSM-IV diagnoses by case for the COPD group and clinical control group (CCG) (listed are only those participants who received a diagnosis).

Group	Current principal diagnosis	Current co-morbid diagnosis	Prior history
COPD case code			
1	Panic disorder with agoraphobia		Generalized anxiety disorder
2	Panic disorder with agoraphobia	Specific phobia	
3	Panic disorder with agoraphobia	Posttraumatic stress disorder	
6	Specific phobia (situational type)		Generalized anxiety disorder
8	Social phobia		Panic disorder without agoraphobia, nicotine use disorder, major depressive disorder
9	Panic disorder with agoraphobia	Nicotine use disorder	
14	Specific phobia (situational type)		Major depressive disorder
16	Panic disorder with agoraphobia		
17	Panic disorder with agoraphobia	Dysthymic disorder	
18	Panic disorder with agoraphobia		
19	Panic disorder with agoraphobia	Social phobia	Nicotine use disorder, hypochondriasis
CCG case code			
23			Dysthymic disorder
24	Alcohol use disorder		
25	Specific phobia (blood-injection-injury type)		
26	Panic disorder with agoraphobia	Specific phobia	Major depressive disorder
30			Panic disorder, dysthymic disorder
32	Pain disorder		
34			Major depressive disorder
38	Panic disorder without agoraphobia		
39	Social phobia		Major depressive disorder

comparisons of SCL-90-R factors yielded significant group differences for somatization, depression, anxiety and phobic anxiety, with COPD patients scoring reliably higher on these scales than CCG participants. COPD patients also showed two significantly higher global indices (global severity score, positive symptom distress) and a trend for a higher positive symptom total score, indicating higher overall psychological symptom distress in the COPD group compared with the CCG group. Univariate comparisons of SISS scales revealed significantly higher scores for COPD patients on all symptom perception scales ($p \leq 0.001$) with the exception of musculoskeletal symptoms, suggesting an almost uniformly more intense perception of physical symptoms in the COPD group compared with CCG participants. In post hoc analyses of covariance using anxiety levels (SCL-90-R sub-scale Anxiety) as covariate and the total symptom perception score as dependent variable the main effect for group remained ($p < 0.001$).

Differences between COPD patients with and without anxiety disorder

Group comparisons between COPD patients with and without a DSM-IV diagnosis of anxiety disorder were carried out on measures of pulmonary function, agoraphobic and panic cognitions, symptom perception and perceived breathless-

ness. Descriptive statistics and error probabilities are summarized in Table 4. MANOVA including pulmonary function parameters, SISS scales (excluding total symptom perception score) and perceived breathlessness revealed a significant main effect for group ($p < 0.01$). Univariate comparisons produced no differences in lung function parameters suggesting similar levels of disease severity in COPD patients with and without anxiety disorder. However, groups differed significantly in their perception of physical symptoms as measured by the SISS: COPD patients with anxiety disorder diagnosis reported higher levels of perception of cardiovascular, gastrointestinal, respiratory and overall symptoms than COPD patients without anxiety disorder diagnosis (all $p < 0.001$). Also, reliably more COPD patients with anxiety disorder diagnosis reported agoraphobic and panic cognitions (fear of fear, fear of dying) during an episode of acute breathlessness than those without anxiety disorder ($p < 0.05$ and 0.001). In contrast, more COPD patients without anxiety disorder endorsed thoughts of "seeking help" during such an attack ($p < 0.01$). Groups did not differ in their level of perceived breathlessness. Multiple regression analyses with the anxiety scale of the SCL-90-R as dependent variable and the total symptom perception score of the SISS and agoraphobic/panic cognitions (fear of fear, fear of dying) as independent variables showed that anxiety levels could be predicted with a multiple $r = 0.41$, ($p < 0.05$).

Table 3 Mean (S.D.) SCL-90-R and SISS results for the COPD group and clinical control group (CCG).

	COPD (n = 20)	CCG (n = 20)	p-Value
SCL-90-R			
Somatisation	1.34 (0.1)	0.88 (0.4)	0.02
Obsessive-compulsive	0.85 (0.5)	0.64 (0.4)	0.19
Interpersonal sensitivity	0.46 (0.4)	0.33 (0.3)	0.28
Depression	0.76 (0.4)	0.42 (0.3)	0.01
Anxiety	0.97 (0.5)	0.38 (0.2)	0.001
Hostility	0.41 (0.3)	0.26 (0.2)	0.08
Phobic anxiety	0.57 (0.4)	0.17 (0.2)	0.001
Paranoid ideation	0.49 (0.5)	0.36 (0.4)	0.41
Psychoticism	0.25 (0.2)	0.18 (0.2)	0.34
Global severity index	0.74 (0.3)	0.37 (0.2)	0.006
Positive symptom distress	1.70 (0.4)	1.41 (0.2)	0.01
Positive symptom total	37.5 (13.7)	28.6 (15.3)	0.06
SISS			
Cardiovascular symptoms	4.1 (1.1)	2.1 (0.9)	0.001
Gastrointestinal symptoms	4.3 (1.4)	2.6 (1.4)	0.001
Musculoskeletal symptoms	4.1 (1.7)	3.1 (1.8)	0.09
Respiratory symptoms	4.8 (2.5)	2.25 (1.2)	0.001
Total symptom perception	4.3 (1.0)	2.51 (0.9)	0.001

SCL-90-R, Symptom Checklist-90-Revised (range: 0–4); SISS, Self-Report Inventory for Somatic Symptoms (range: 1–7).

Discussion

The aims of the current study were to assess mental disorders in hospitalized patients with COPD and to identify moderating factors explaining any mental co-morbidity. In contrast to most previous studies investigating mental disorders in this patient group we used a standardized clinical interview employing DSM-IV criteria and compared results with a hospitalized CCG in order to test for specificity of mental disorders in COPD. Results indicated higher overall psychological symptom distress in COPD patients compared with the CCG with 55% of COPD patients receiving a current principal DSM-IV diagnoses compared to 30% in the CCG. These findings were mirrored by the results from a questionnaire measure (SCL-90-R). All current diagnoses in the COPD group were anxiety disorders ($n = 11$) which differed significantly from the number of anxiety disorders in the CCG ($n = 4$). By far the most common type of anxiety disorder in the COPD group was Panic Disorder with Agoraphobia accounting for almost three quarters of all (anxiety) diagnoses awarded. In contrast, not only were

Table 4 Mean (S.D.) pulmonary function, symptom perception, agoraphobic and panic cognitions, perceived breathlessness and perceived and actual level of COPD information for COPD patients with and without a principal anxiety disorder diagnosis.

	COPD with anxiety (n = 11)	COPD without anxiety (n = 9)	p-Value
Pulmonary function			
FEV ₁ /VC (%)	61.64 (5.9)	60.94 (6.4)	ns
r_{tot} (kPa/l/s)	0.62 (0.26)	0.67 (0.23)	ns
PaO ₂ (mmHg)	63.78 (8.9)	64.98 (7.6)	ns
SISS			
Cardiovascular symptoms	4.9 (0.7)	3.2 (0.9)	<0.001
Gastrointestinal symptoms	5.2 (0.7)	3.2 (1.2)	<0.001
Musculoskeletal symptoms	4.0 (1.6)	4.2 (1.9)	ns
Respiratory symptoms	6.0 (0.8)	3.2 (1.2)	<0.001
Total symptom perception	5.0 (0.7)	3.4 (0.7)	<0.001
Agoraphobic/panic cognitions			
Fear of fear	Yes: 8, No: 3	Yes: 2, No: 7	<0.05
Fear of dying	Yes: 10, No: 1	Yes: 0, No: 9	<0.001
Stay calm	Yes: 5, No: 6	Yes: 3, No: 6	ns
Seek help	Yes: 0, No: 11	Yes: 5, No: 4	<0.01
Perceived breathlessness			
Visual analog scale (0–12)	11.0 (7.7)	9.9 (2.8)	ns
Information level			
Perceived (1 = good, 2 = medium, 3 = poor)	1.6 (0.6)	1.4 (0.5)	ns
Actual (range 0–14)	7.0 (3.7)	7.0 (3.5)	ns

FEV₁/VC (%), ratio of forced expiratory volume in 1 s to vital capacity (%); r_{tot} , airway resistance; PaO₂, partial pressure of arterial oxygen; SISS, Self-Report Inventory for Somatic Symptoms (range: 1–7).

there a fewer number of anxiety disorder cases in the CCG; there was also a more heterogeneous mix of anxiety disorder sub-types with no more than one case per diagnosis. These elevated levels of anxiety in the COPD group were corroborated by higher scores on the SCL-90-R sub-scales Anxiety and Phobic Anxiety.

Our results are in line with previous studies reporting elevated levels of anxiety disorders in patients with COPD,^{6–19} with estimates ranging from 2% to 51% as outlined in previous systematic reviews.^{18,19} The factors contributing to this wide range of prevalence estimates are not clear but most probably include differences in assessment methods,

the in- or outpatient status of study participants, and the heterogeneity in primary medical diagnoses (COPD, Asthma or both). With 55% the rate observed in the current study is at the top end of this distribution. Although the small sample size and the inclusion of patients with mild to moderate COPD during symptom exacerbation episodes limits any more wide-ranging conclusions about prevalence rates of anxiety disorders in the whole population of patients with COPD, these results indicate that anxiety disorders in general and Panic Disorder with Agoraphobia in particular are common among hospitalized patients with COPD. Most importantly, the difference in the pattern of diagnoses between the examined hospitalized patient groups suggests that anxiety disorders are more specific to COPD when compared with other chronic physical disorders such as orthopaedic conditions, which already show higher prevalence rates of anxiety disorders when compared to the healthy population.³⁴ Thus, the experience of a chronic medical condition or a related hospitalization per se cannot completely explain the high prevalence of anxiety among these patients with COPD.

In addition to current diagnoses the clinical interview used in the current study allowed for the retrospective assessment of prior history of mental disorders. Although the number of past diagnoses was identical for both groups, there was a significant association between past and current diagnoses in COPD patients only. In other words, those COPD patients who had a DSM-IV diagnosis in the past were more likely to receive a current diagnosis; this was not the case in the CCG. This finding in combination with the obtained high specificity of anxiety disorders in the COPD group raises the important question of whether anxiety in COPD is a consequence of COPD or whether anxiety can also precede COPD and is, therefore, somehow implicated in the etiology of this disorder. There is evidence that the lifetime prevalence of respiratory disease is higher in people with panic disorder compared to other mental disorders.³⁵ Further, in a sample of 515 relatively young adults, who had participated in the European Commission Respiratory Health Survey (ECRHS) I and II,^{36,37} Neuman et al. found that in subjects without dyspnea at the first survey the onset of anxiety was significantly related to having dyspnea at the second survey, i.e. 9 years later.³⁸ In contrast, the onset of dyspnea at the first survey was not associated with developing anxiety at the second survey. However, due to significant interactions with depressive symptoms and the sole use of questionnaire measures the authors conclude that no firm effect-relationship between psychological status and dyspnea could be derived. The retrospective design of the current study does not allow for the exact establishment of the sequence of the onset of disorders. However, the present results warrant further investigation of the interaction of respiratory disease and anxiety disorders.

Based on previous findings,^{6,7,18} we also expected depression rates to be higher in COPD patients than in the CCG. This was confirmed in that the former reported higher depression scores on the relevant SCL-90-R scale compared to the latter. However, based on the clinical interview there were no current principal DSM-IV diagnoses of major depression or any other mood disorder in either group except for one case of co-morbid dysthymic disorder in the

COPD group. Van Manen et al.'s⁷ findings suggest a non-linear association between depressive symptoms and measures of pulmonary function in that clinically relevant depression scores were found only in patients with severe airways obstruction. In addition, factors such as living alone and self-reported impaired physical function mediated this relationship. Lung function test results obtained for COPD patients in the current study indicate a mild-to-moderate level of disease severity. Taken together with the fact that the majority of patients in the current study were living with a partner, these differences in disease severity and living status might explain the lack of any clinical principal depression diagnoses. Alternatively, the use of a clinical interview instead of questionnaire measures might have prevented false positive diagnoses, suggesting that studies examining the mental status in patients with COPD should rather include diagnostic interviews than solely use questionnaires.

Our results from the SISS suggest a more intense perception of physical symptoms in COPD patients not only of respiratory symptoms but extending to the gastrointestinal and cardiovascular systems compared with CCG participants. Because of the nature of their disease COPD patients have ample opportunity to experience symptoms of physiological distress. It seems noteworthy, however, that heightened symptom perception should generalize to body systems other than the one primarily affected by COPD, i.e. the respiratory system. Results from the comparison of COPD patients with and without anxiety disorder further suggest a higher level of symptom perception in the former. This converges with findings by Put et al.³⁹ showing that asthmatic patients with high negative affectivity (which includes increased levels of anxiety) reported overall more respiratory and other symptoms compared to patients with low negative affectivity, which was unrelated to pulmonary status. In psychophysiological models of anxiety and in particular panic²¹ it is assumed that the more accurate and more intense perception of cardiac activity leads to catastrophic misinterpretations of physical symptoms and, therefore, feeds into a vicious circle of panic (increase in arousal, more intense perception, catastrophic misinterpretation, more physical symptoms, etc). Similarly, in somatization disorder a body-related perceptual style has been described ("somatic amplification")⁴⁰ which is assumed to be grounded on selective attention to physical symptoms. However, whether the more accurate perception of physical symptoms is a prerequisite for their more intense experience is unclear, and the evidence on better (i.e. more accurate) physical symptom perception in patients with panic disorder is inconclusive.⁴¹ Results from the current study suggest a contributing role of physical symptom perception to anxiety levels; however, after controlling for the effects of anxiety levels the group difference between COPD and CCG remained confirming the notion of a more intense general perception of physical symptoms in patients with COPD. Alternatively, it could be argued that individuals who experience panic disorder are likely to experience elevated levels of these kinds of symptoms (but not musculoskeletal symptoms). In other words, the elevated symptoms may not be related to the respiratory disorder, but instead reflect the panic symptoms (perhaps even the respiratory symptoms).

In addition to higher levels of symptom perception in COPD patients with anxiety disorders, the number of patients reporting agoraphobic and panic cognitions during an acute episode of breathlessness was higher in this group compared with COPD patients without anxiety disorders. These findings, in conjunction with the lack of difference in actual respiratory function or perceived breathlessness are consistent with the hypothesis that anxiety in COPD patients is the result of negative cognitions and symptom perception rather than actual or perceived respiratory distress. Similar findings have been reported in previous studies demonstrating that health-related quality of life in COPD patients is mostly unrelated to objective respiratory measures.^{42–44} This was confirmed in that anxiety levels could be predicted by both symptom perception and negative cognitions. It is noteworthy in this context that perceived breathlessness (“How much do you suffer from breathlessness?”) did not differ between anxiety groups whereas symptom perception (“To what extent are you aware of symptoms from your lungs?”) did. This suggests that the experience of breathlessness and the extent to which individuals are aware of respiratory symptoms are independent and only the latter contributes to anxiety. If being aware of physical symptoms reflects the selective allocation of attention this perceptual style would be reminiscent of “somatic amplification”³³ as described for somatization disorder.

More than half of COPD patients without anxiety disorder reported thoughts of seeking help during an acute episode of breathlessness as opposed to none in those with anxiety disorder. This seems to indicate that “seeking help” may be a positive cognitive or behavioral coping strategy possibly leading to an increased sense of control and, therefore, preventing increases in anxiety and catastrophic misinterpretations of physical symptoms. However, these results should be considered as preliminary and, therefore, in need of replication in future research as the questionnaire used was self-constructed with yet unknown psychometric properties.

Clinical implications

Recent reports have emphasized the role of mental factors on the course of disease in respiratory disorders.^{12,13,45} In particular anxiety and negative affectivity have been suggested to be associated with inadequate medication use,⁴⁶ frequent visits to the physician,⁴⁷ increased number and duration of hospitalizations,^{23,48} patients’ treatment preferences⁴⁹ as well as increased mortality, symptom burden, and poorer physical and social functioning.⁴⁸ The findings of the current study have, therefore, implications for interventions designed to reduce symptoms, increase functioning, and improve COPD patients’ quality of life. First and foremost, our results with improved methodology confirm that anxiety disorders are common among hospitalized patients with COPD, thus, underlining the importance of screening for mental disorders in this patient group. By far the most common anxiety disorder in the current study was Panic Disorder with Agoraphobia. The treatment procedure of choice for Panic Disorder with Agoraphobia is cognitive-behavioral treatment which typically involves cognitive restructuring, interoceptive exposure and re-

peated confrontation with, or approach to, the object or situation that is avoided. Given the evidence for the efficacy of exposure-based treatments,⁵⁰ it is tempting to conclude that this approach should also be used in the treatment of anxiety disorders in COPD patients. However, cognitive restructuring will have to strike a very tenuous balance between proper monitoring of physical symptoms that could signal actual danger while reducing catastrophic misinterpretation of benign physical sensations. It should be noted in this context that this problem is not unique to COPD but applies also to other chronic conditions, e.g. chronic pain. Perhaps helpful in finding this equilibrium between appropriate monitoring and hypervigilance while also improving mobility could be targeting the agoraphobic avoidance that seems to be prevalent among anxiety disordered COPD patients. Agoraphobic avoidance is specified in the DSM-IV nosology as avoidance, or endurance with distress, of situations from which escape might be difficult or in which help is unavailable in the event of a panic attack or of developing symptoms that could be incapacitating or embarrassing.²⁶ Typical situations that are avoided include shopping in malls, waiting in lines, attending movie theatres, traveling by car or bus, visiting crowded restaurants and stores, and being alone. Successful reduction of agoraphobic avoidance through exposure techniques would almost certainly lead to the mobilization of anxiety disordered COPD patients thus increasing their physical activity. High levels of physical activity, in turn, have been shown to be associated with a 46% reduction in the risk of hospital readmission in COPD patients.⁵¹ First encouraging findings were recently reported by Kunik et al.⁵² suggesting that as little as two hours of group therapy containing elements of cognitive-behavioral therapy can lead to a reduction of symptoms of depression and anxiety compared to a control group who only received patient education. However, future studies with randomized controlled designs and longer-lasting programs are necessary to testify the effects of cognitive-behavioral treatments for reducing anxiety as well as improving symptom management in patients with COPD.^{53,54}

Limitations of the current study

Besides the limited sample size and the exclusive investigation of patients with mild-to-moderate COPD admitted to hospital because of exacerbation episodes, it cannot be ruled out that the age difference between our study groups may have impacted on the results. However, it seems unlikely that the higher number of anxiety disorder diagnoses in the COPD group could be explained by the older age in this group, as the main age of onset for Panic Disorder with Agoraphobia lies between adolescence and the mid-30s. Any age-related increase in prevalence should have occurred before the mean age of the current two groups. This view was supported by an additional set of analyses including age (and also gender) as covariates, which yielded no meaningful differences to the reported results. Moreover, patients with co-morbid conditions (e.g., coronary heart disease, stroke, dementia) were excluded, because these conditions have been shown to be associated with increased levels of anxiety and depression, which could have added to

psychological impairments unrelated to COPD. Because coronary heart disease is common in patients with COPD this exclusion could somewhat limit the generalizability of our results. Further, we cannot completely rule out that some of the psychological symptoms in the patients history occurred during exacerbation periods, e.g. due to incomplete medical charts. However, this seems rather unlikely due to the careful assessment of these prior symptoms in a threefold way: by interview, by crosschecking the medical records and by discussing all symptoms with a physician.

In addition, the design of the study does not allow for cause and effect relationships between COPD and mental disorders to be firmly established. While it appears that symptom perception and catastrophic interpretations of bodily symptoms play a role in the onset of anxiety symptoms in COPD, this cannot be conclusively stated due to the retrospective nature of the current study design. Future investigations of etiologically relevant factors will, therefore, benefit from well-controlled prospective designs.

Conflict of interest statement

There is no potential conflict of interest related to the article or the research described.

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